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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,347	11/09/1999	CHRISTINE A. WHITE	27693-01201	6491

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SIDLEY AUSTIN LLP
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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

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02/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/436,347	WHITE ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/01/2008 & 02/05/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/05/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____ .

DETAILED ACTION

Response to Arguments

1. Claims 29-97 are pending.

Claims 29-97 are examined on the merits.

Maintained Grounds of Rejection

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The rejection of claims 29-97 under 35 U.S.C. 103(a) as being unpatentable over IDEC Pharmaceuticals Corp. (1997/ IDS reference D158 submitted July 9, 2007), and further in view of U.S. Patent number 5,843,398 (filed April 26, 1996/ IDS reference D18 submitted July 9, 2007), U.S. Patent Application Publication number 2003/0018014 A1 (effective filing date September 17, 1998) and Stenbygaard et al. (Breast Cancer Research and Treatment 25: 57-63, 1993) is maintained.

Applicants have set forth arguments in a single discussion given their assertion "[t]he teachings of the three primary references...serve comparable functions..., as do the collective teachings of the remaining references.", see last paragraph on page 2 of the Remarks submitted December 1, 2008. Applicants have also submitted a declaration under 37 C.F.R. § 1.132 of David P. Schenkein, M.D.

Applicants assert "[t]he primary references describe the use of rituximab to treat non-Hodgkin's lymphoma" and do not refer to the treatment of CLL, see page 3. Applicants aver the differences between CLL and NHL diseases and "[t]he references do not demonstrate a reasonable expectation of success for practicing the claimed invention", see pages 5 and 6. Applicants further assert "[n]one of the additional references suggest using a CD20 antibody to treat CLL", see page 3 of Remarks. One of those additional references, according to Applicants, the Kaminski patent (U.S. patent number 5,843,398) describes the use and the benefits of a therapeutic radiolabeled antibody in view of the "limited efficacy of unmodified antibodies" and "…do not relate to the use of a CD20 antibody to treat CLL". As for Anderson et al. (U.S. Patent number 5,736,137) Applicants simply aver the reference does not mention CLL and discloses NHL treatment with rituximab and that does not correlate with CLL treatment, see Remarks, page 3, 5th paragraph.

Dr. Schenkein declares CD20 expression is relatively lower on CLL cells than NHL cells and because of such would lead to uncertainty of whether CD20 antibodies could bind to CLL tumor cells, see Declaration, paragraphs 19 and 20. Dr. Schenkein asserts there would be decreased therapeutic efficacy of CD20 antibody because CLL is characterized by a high number of circulating tumor cells, hence the large number of tumor cells would create a "sink" of CD20 antibody-binding sites, see declaration paragraphs 29-31. These points of view, the declaration and accompanying papers have been carefully considered, but found unpersuasive.

While the primary references teach the administration of the CD20 antibody, rituximab to B cell cancer others than CLL, the combination of references does not preclude the instant rejection. Likewise, the declaration under 37 C.F.R. § 1.132 filed December 1, 2008 is insufficient to overcome the rejection under 35 U.S.C. 103(a) because it does not provide a showing of good and sufficient reasons why one of ordinary skill in the art would not be motivated to try implementing a mode of therapy, which has been successful in one B cell cancer treatment, in another B cell cancer treatment.

The Examiner has set forth the relevant teachings of the prior art relied upon indicating relevant column, page and line numbers; the differences in the claim over the references; how the references can be modified to arrive at the claimed method; and why the claimed method would have been obvious to one of ordinary skill in the art at the time the invention was made, see MPEP section 706.02(j). Furthermore, the Examiner has established the suggestion and motivation in the references available to one of ordinary skill in the art to combine the references. The IDEC Pharmaceuticals Corp. reference speaks to the applicability of implementing combination therapy comprising rituximab and CHOP to patients with CD20 positive cancers. While Applicants note the McLaughin reference specifically excludes CLL patients, that seems to be more a reflection of streamlining the patient population for testing and not a reflection of inefficiency of treatment to the CLL patient population, see page 3, 4th paragraph of Remarks. There is no factual evidence presented in McLaughin or by Applicants and Declarant teaching one or ordinary skill in the art not to try to implement

CD20 antibody therapy in the CLL population. Anderson teaches therapeutic methods designed for the general treatment of B cell disorders including CLL, see column 5, Summary...section. Anderson does teach with particularity treatment of B cell lymphomas, however that in and of itself does not teach away from using the taught anti-CD20 antibody for CLL treatment.

Second, there must be a reasonable expectation of success which is presented in all the references, particularly the Kaminski patent, which plainly and clearly teaches the effectiveness of CD20 therapy for a B cell cancer and the high expression of CD20 antigen on CLL (more than 95% expression on patients with CLL), see patent, column 8, lines 9-16. And while both Kaminski patents do teach CD20 antibody therapy directed to B-cell lymphoma as Applicants point out this does not teach away from the combination of the references. The Kaminski patents, both cite Example IV wherein unlabeled CD20 antibody is used in combination with chemotherapy, hence they patents do not just describe the use of therapeutic radiolabeled antibody as suggested by Applicants.

Lastly, the references when combined do teach or suggest all the claim limitations. It would be obvious to one of skill in the art to implement a potential method for successful CLL treatment in light of rituximab has been administered to other B cell patients with relapsed and refractory B cell cancers, see declaration paragraphs 24-27. While the declarant suggests there would be decreased therapeutic efficacy that suggestion is not equivalent to there would be *no* therapeutic effectiveness. There seems to be no factual evidence presented suggestive of failure of treatment of CLL in a

patient. Applicants are reminded the term, treatment reads broadly on a process of implementing therapy to modify, alter or remedy a health problem. Differences between CLL and NHL do not teach away from the desirability of doing what the inventor has done. Applicants and Declarant have not presented sufficient evidence teaching the immunotherapeutic mechanisms, host effector functions and receptor binding affinity of the CD20 antibody would differ between the two diseases, resulting in different antitumor mechanisms and significant differences in the impact of the therapy. There is adequate and sufficient teachings and suggestion in all the references to make the claimed combination with a reasonable expectation of success. This rejection is maintained for the reasons of record and the analysis set forth herein.

8. The rejection of claims 29-97 under 35 U.S.C. 103(a) as being unpatentable over McLaughin et al. (Journal of Clinical Oncology 16(8): 2825-2833, August 1998/ IDS reference B1, submitted October 19, 2007), and further in view of U.S. Patent number 5,843,398 (filed April 26, 1996/ IDS reference D18 submitted July 9, 2007), U.S. Patent number 6,090,365 (filed November 18, 1997/ IDS reference D20 submitted July 9, 2007), U.S. Patent Application Publication number 2003/0018014 A1 (effective filing date September 17, 1998) and Stenbygaard et al. (Breast Cancer Research and Treatment 25: 57-63, 1993) is maintained.

As noted in the first cited 103 rejection Applicants have set forth arguments in a single discussion given their assertion "[t]he teachings of the three primary references...serve comparable functions..., as do the collective teachings of the

remaining references.", see last paragraph on page 2 of the Remarks submitted December 1, 2008. The Examiner has presented the rebuttal of those arguments and declaration in the same manner, a single discussion. The response to the traversal of the instant rejection is the same as that presented in paragraph 7. This rejection is maintained for the reasons of record and the analysis set forth herein.

9. The rejection of claims 29-42 and 44-97 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,736,137 (filed November 3, 1993/ IDS reference HR submitted May 19, 2004), and further in view of U.S. Patent number 5,843,398 (filed April 26, 1996/ IDS reference D18 submitted July 9, 2007), U.S. Patent number 6,090,365 (filed November 18, 1997/ IDS reference D20 submitted July 9, 2007) and Stenbygaard et al. (Breast Cancer Research and Treatment 25: 57-63, 1993) is maintained.

As noted in the first cited 103 rejection Applicants have set forth arguments in a single discussion given their assertion "[t]he teachings of the three primary references...serve comparable functions..., as do the collective teachings of the remaining references.", see last paragraph on page 2 of the Remarks submitted December 1, 2008. The Examiner has presented the rebuttal of those arguments and declaration in the same manner, a single discussion. The response to the traversal of the instant rejection is the same as that presented in paragraph 7. This rejection is maintained for the reasons of record and the analysis set forth herein.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, Monday through Saturday with alternate Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
11 February 2009

/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643